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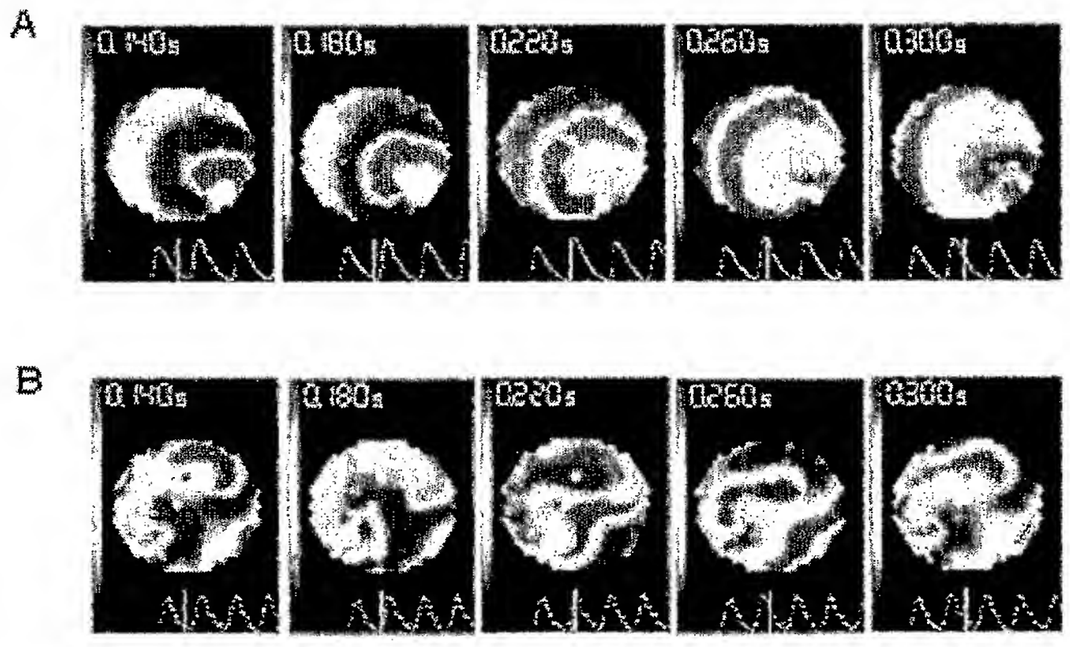
(54) Title: PREVENTING ARRHYTHMIAS ASSOCIATED WITH CELL TRANSPLANTATION



(57) Abstract: Skeletal myoblasts are an attractive cell type for transplantation since they are autologous and resistant to ischemia. However, clinical trials of myoblasts transplantation in heart failure have been plagued by ventricular tachy-arrhythmias and sudden cardiac death. The pathogenesis of these arrhythmias is poorly understood, but may be related to the fact that skeletal muscle cells, unlike heart cells, are electrically isolated by the absence of gap junctions. An in vitro model of myoblasts transplantation into cardiomyocyte monolayers can be used to investigate the mechanisms of transplant-associated arrhythmias. Co-cultures of human skeletal myoblasts and rat cardiomyocytes result in reentrant arrhythmias (spiral waves) that reproduce the features of ventricular tachycardia seen in patients receiving myoblasts transplants. These arrhythmias can be terminated by nitrendipine, an L-type calcium channel Mocker, but not by the Na channel blocker lidocaine. Genetic modification of myoblasts to stably express the gap junction protein connexin 43 decreases arrhythmogenicity in co-cultures. It similarly can be used to increase the safety of myoblasts transplantation in patients.

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